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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/536,834

03/20/2006

Steffen Goletz

GULDE-59

7472

24997

7590

02/19/2009

MILLEN, WHITE, ZELANO & BRANIGAN, PC

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EXAMINER

CANELLA, KAREN A

ART UNIT

PAPER NUMBER

1643

MAIL DATE

DELIVERY MODE

02/19/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/536,834

Applicant(s)

GOLETZ ET AL.

Examiner

Karen A. Canella

Art Unit

1643

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 74-84 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☐ Claim(s) 74-84 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SF/08)
Paper No(s)/Mail Date 5/31/05 3/20/06
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date ____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: ____

DETAILED ACTION

Please note that the examiner assignment to this application has changed.

Acknowledgement is made of applicant's election of Group I and the Species of SEQ ID NO:1, 4, 7, 10, 12, 47, 50, 80 and 81. After review and reconsideration, both the Restriction Requirement and the Election of Species Requirement, mailed June 23, 2008 is withdrawn.

Claim 76 has been amended. Claims 74-84 are pending and examined on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 76 and 79 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of “variable heavy chain” and “variable light chain” in claim 76 lacks specific antecedent basis in claim 74.

Claim 79 is vague and indefinite in the recitation of MHC class I or Class II antigens. It is unclear if the antigen is the peptide displayed in the context of the MHC, or if the antigen is the MHC protein itself.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 74, 76, 78-84 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not

described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re wands, 858 F.2d 731, 737.8 USPQ2d 1400, 1404 (Fed. Cir. 1988)..

(A) As drawn to a recognition molecule comprising only three hypervariable regions of the heavy chain..

Claims 74 is drawn to a recognition molecule comprising an amino acid sequence which comprises SEQ ID NO:1, SEQ ID NO:2 or 3 and SEQ ID NO:4, 5 or 6, wherein said molecule specifically binds the core 1 antigen. Claim 79 is drawn to a construct comprising the recognition molecule of claim 74; claim 80 is drawn to a method fro the production of the recognition molecule of claim 74 Claims 81-84 are methods reliant on the identity o the recognition molecules of claims 74 and 79. The specification teaches that the recognition molecules of the instant invention were derived from the scFv molecule of SEQ ID NO:95 (page 57, example 1). Thus the recognition molecules contain hypervariable domains and variable domains consistent with their origins in the single chain antibody molecule. When given the broadest reasonable interpretation, claim 74 encompasses a molecule comprising only three of the hypervariable regions of the heavy chain. Claim 78 encompasses claim 74 wherein the molecule is a "fusion protein of an antibody fragment with peptides or proteins" and thus also encompasses an antibody fragment comprising less than the full antibody paratope comprising the full complement of three heavy chain hypervariable regions and three light chain hypervariable regions..

Claim 76 encompasses additional heavy chain variable region sequence that fall between the CDR sequences of claim 74, but fails to provide for more than the three CDR sequences. Claims 78-84. Claim 78 comprises a construct of the recognition molecule of claim 74, but fails to provide for more than the three CDR sequences. Claims 80-84 are method claims encompassing the recognition molecules of claim 74.

It is well established in the art that the formation of an intact antigen-binding site generally requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs which provide the majority of the contact residues for the binding of the antibody to its target epitope. The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity which is characteristic of the parent immunoglobulin. It is expected that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites. Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff et al (Proc Natl Acad Sci USA 1982 Vol 79 page 1979). Rudikoff et al. teach that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function. It is unlikely that fusion proteins as defined by the claims which may contain less than the full complement of CDRs from the heavy and light chain variable regions of an IL-1 β antibody in unspecified order and fused to any human or nonhuman framework sequence, have the required binding function. The specification provides no direction or guidance regarding how to produce fusion proteins and antibodies as broadly defined by the claims. Undue experimentation would be required to produce the invention commensurate with the scope of the claims from the written disclosure alone. Further, the specification does not teach that a functional humanized antibody can be obtained by replacing the CDR regions of an acceptor antibody with the CDRs of a donor antibody. As evidenced by Adair et al. (PCT GB90/02017) transfer of CDR regions alone are often not sufficient to provide satisfactory binding activity in the CDR-grafted product (p. 4). Panka et al (Proc Natl Acad Sci USA Vol 85 3080-3084 5/88) demonstrate that a single amino acid substitution of serine for alanine results in decreased affinity.

While there are some publications which acknowledge that CDR3 is important, the conformations of other CDRs as well as framework residues influence binding. MacCallum et al. (Journal of Molecular. Biology, 1996, Vol 262, pp. 732-745), analyzed many different

antibodies for interactions with antigen and state that although CDR3 of the heavy and light chain dominate, a number of residues outside the standard CDR definitions make antigen contacts (see page 733, right column) and non-contacting residues within the CDRs coincide with residues as important in defining canonical backbone conformations (see page 735, left col.).

Pascalis et al (Journal of Immunology, 2002, Vol. 169, pp. 3076-3084) demonstrate that grafting of the CDRs into a human framework was performed by grafting CDR residues and maintaining framework residues that were deemed essential for preserving the structural integrity of the antigen binding site (see page 3079, right col.). Although abbreviated CDR residues were used in the constructs, some residues in all 6 CDRs were used for the constructs (see page 3080, left col.).

The fact that not just one CDR is essential for antigen binding or maintaining the conformation of the antigen binding site, is underscored by Casset et al (Biochemical and Biophysical Research Communications, 2003, Vol. 307, pp. 198-205), which constructed a peptide mimetic of an anti-CD4 monoclonal antibody binding site by rational design and the peptide was designed with 27 residues formed by residues from 5 CDRs (see entire document). Casset et al. also states that although CDR H3 is at the center of most if not all antigen interactions, clearly other CDRs play an important role in the recognition process (page 199, left col.) and this is demonstrated in this work by using all CDRs except L2 and additionally using a framework residue located just before the H3 (see page 202, left col.).

Vajdos et al. (Journal of Molecular biology, 2002, Vol. 320, pp. 415-428), additionally state that antigen binding is primarily mediated by the CDRs more highly conserved framework segments which connect the CDRs are mainly involved in supporting the CDR loop conformations and in some cases framework residues also contact antigen (page 416, left col.).

Holm et al (Molecular Immunology, 2007, Vol. 44, pp. 1075-1084) describes the mapping of an anti-cytokeratin antibody where although residues in the CDR3 of the heavy chain were involved in antigen binding unexpectedly a residue in CDR2 of the light chain was also involved (abstract).

Chen et al. (Journal of Molecular Biology, 1999, Vol. 293, pp. 865-881) describe high affinity variant antibodies binding to VEGF wherein the results show that the antigen binding

site is almost entirely composed of residues from heavy chain CDRs, CDR-H1, H2, H3 (page 866).

Wu et al. (Journal of Molecular Biology, 1999, Vol. 294, pp. 151-162) state that it is difficult to predict which framework residues serve a critical role in maintaining affinity and specificity due in part to the large conformational change in antibodies that accompany antigen binding (page 152 left col.) but certain residues have been identified as important for maintaining conformation.

One of skill in the art would neither expect nor predict the appropriate functioning of the antibody as broadly as is claimed. It is suggested that the specific portion of the human constant region, which the variable region is covalently linked to, be explicitly recited within the claim or this language be removed completely in order to obviate this rejection. Therefore, in view of the lack of guidance in the specification and in view of the discussion above one of skill in the art would be required to perform undue experimentation in order to practice the claimed invention as it pertains to .

(B) As drawn to constructs which are attached to enzyme molecules, interaction domains, domains for stabilization, catalytic antibodies, immunomodulators, MHC Class I or class II antigens, transmembrane domains, viruses or cells.

Claim 79 is drawn in part to a recognition molecule, which is covalently or non-covalently associated with domains for stabilization, catalytic antibodies, MHC class I or class II antigens, viruses or cells. First, it is unclear how a molecule which is associated with another molecule by a non-covalent interaction, such as an ionic or Van Der-Waals interaction can maintain said association after administration in vivo. Secondly, the specification fails to teach "enzyme molecules" which would be effective cargo to be transported to the targeted cancer cells by the recognition molecules of the invention. The art teaches "ADEPT" which is an antibody directed pro-drug therapy which relies on a concentration gradient of proteolytic enzymes released from a tumor to catalytically activate a prodrug to a drug in the environs of tumors (Bagshawe et al, Expert Opin Biol Ther. 2004, Vol. 4, pp. 1777-1789).. However, in the instant case, the enzyme is being transported by the recognition molecule. Therefore it is unclear how this transported enzyme is to be efficacious in tumor reduction since the recognition molecule is supplying the enzyme rather than the pro-drug. Further, the art teaches DNase can be

conjugated to antibodies and transported to target sites (abstract of Linardou). However, it is required that the DNase be internalized into the target cell (lines 7-9 of abstract). The instant specification provides no objective evidence that the core 1 antigen undergoes endocytosis in the tumor cell and could serve as an internalizing antigen for the transport of enzymes which serve to degrade the tumor cell after uptake. Claim 79 is drawn in part to recognition molecule covalently or non-covalently associated with a domain for stabilization. The specification provides no teaching as to what the stability is in reference to, such as a mutant constant region leading to increased half life in circulation (Presta et al, U.S. 5,739,277), or if the stabilization was some other type of stabilization. Claim 79 is drawn in part to the recognition molecule covalently or non-covalently associated with a catalytic antibody. The specification has failed to teach a molecule which requires catalysis in the context of the extracellular environment of a tumor as there is no evidence that the core-1 antigen undergoes endocytosis to the cytoplasm. Thus, without the target for the catalysis, one of skill in the art would be subject to undue experimentation in order to make and use the construct comprising catalytic antibodies (Hsieh et al, Science, 1993, vol. 260, pp. 337-339). Claim 79 is drawn in part to MHC class I or class II antigens. The specification provides no teachings as to how to use the transport of an empty MHC I or II receptor or peptides that bind in the context of the MHC targeted to a cancer cell via the instant recognition molecules. T cells recognize peptides presented in the context of an MHC molecule on the surface of a cell. T cells exposed to peptides which are not presented by antigen presenting cells in the context of the MHC leads to T cell death (Matzinger, Annual Review in Immunology, 1994, Vol. 12, pp. 991-1045, page 998, lines 5-11 and page 1001, lines 8-16). Thus, it is unclear how to use a construct comprising these antigens for inducing tumor reduction. Claim 79 is drawn in part to a recognition molecule covalently or non-covalently associated with a transmembrane domain. The specification states that the fusion of an scFv with a transmembrane domain, such as that found in c-erbB2, PDGF receptor, human transferrin receptor or human asialoglycoprotein receptor enable the expression for the binding molecules on the surface of the cells. The art teaches that the presence of the transmembrane domain allows for the stabilization of a protein in the cell membrane after transport through the cytoplasm rather than secretion of said protein (Schneider et al, FEBS Lett, 2002, vol. 532, pp. 231-236). However, there is no objective evidence that the converse, insertion into the cell

membrane after contact with the cell membrane from the extracellular milieu, would lead to insertion of the recognition molecule comprising the transmembrane domain into the cell surface. Claim 79 is drawn in part to a recognition molecule covalently or non-covalently associated with a virus. The specification fails to teach how to use the recognition molecule when conjugated to a virus. there is no reasonable expectation that binding of the recognition molecule to a core 1 antigen on the surface of a target cell, wherein said recognition molecule is attached to a virus, will lead to internalization of said virus within the cell. The art teaches that cell surface receptors on hematopoietic cells more often undergo internalization in contrast to non-hematopoietic receptors because hematopoietic cells are more dependent on external growth factors. Thus, given a non-hematopoietic cell, there is no reasonable expectation that binding of a conjugated or fused recognition molecule when bound to a cell surface protein will result in internalization of the conjugated or fused moiety. Thus, without further objective evidence from the specification, one of skill in the art would conclude that the virus attached to the recognition molecule will remain external to the cell. The specification fails to teach how to use the recognition molecule attached to a virus. Claim 79 is drawn in part to a recognition molecule covalently or non-covalently associated with a cell. When given the broadest reasonable interpretation, the term "cells" encompasses multitude of cells and are not limited to phagocytes, such as macrophage and dendritic cells. One of skill in the art would not know how to use the claimed construct comprising cells which are not phagocytic.

The specification fails to address or provide guidance for any of the above issues, Accordingly, one of skill in the art would be subject to undue experimentation in order to make and use the instant constructs.

(C) As drawn to culturing a virus apart from a host cell

Claim 80 is drawn in part to the culturing of a "virus" as a separate entity apart from a host cell. It is well known in the art that viruses require host cells for replication. Without further guidance from the specification regarding how to overcome the barrier of culturing viruses a single agent without the need for a host cell, one of skill in the art would be subject to undue experimentation in order to carry out the claimed method with respect to the culturing of "viruses".

(D) As drawn to prophylaxis or prevention

Claims 81-84 are drawn in part to the prevention of a tumor. when given the broadest reasonable interpretation, the claims encompass the prevention of a tumor in a non-experimental subject, wherein said subject has never had a tumor. The specification fails to provide any objective evidence that the administration of a "recognition molecule" which binds to "core sequence 1" can prevent the occurrence of cancer in such an individual. The specification fails to teach the positive identification of individual who will develop tumors in order to provide the recognition molecules to said individual before said tumors occur

(E)As drawn to the reduction therapy, follow-up or after care or a tumor disease or a metastasis comprising the administration of the recognition molecule of claim 74 wherein the recognition molecule is without a chemotherapeutic agent or therapeutic radionuclide

Claims 81-83 are drawn to the administration of the recognition molecule of claim 74 for the reduction, for the diagnosis, therapy, follow-up or after care of a tumor disease or metastasis. Claim 84 specifies the recognition molecule f claim 79 is administered. The claims encompass the administration of the recognition molecule without attachment to a chemotherapeutic agent or a therapeutic radioisotope. It is noted that claim 79 includes attachment to immunoglobulin domains of various species (i) and immunoeffectors (xii). When given the broadest reasonable interpretation, the claims include the administration of a chimeric antibody having the CDRs of claim 74 and immunoglobulin domains "of various species". Thus, the claim encompass the treatment of tumors by the induction of an anti-idiotypic cascade, ADCC, CDC or AICD as well as the administration of a naked antibody.

The specification fails to teach that administration of the "naked" antibody will be effective for treating breast cancer in a patient.

The specification provides no objective evidence that antibodies will induce ADCC, CDC, or direct cytotoxicity to the target cell effective to treat a patient having a tumor disease or metastasis The art teaches that antibody effector functions are potentiated through the Fc region of the antibody molecule, including the CH2 region for the activation of the complement cascade, but that many extraneous factors including aggregation and potentially an antigen-induced conformational change is required for efficient complement activation (Morrison et al, 'Complement activation and Fc receptor binding by IgG', In: Protein Engineering of antibody Molecules for Prophylactic and therapeutic applications in Man, 1993, Mike Clark, Ed., pages

101-113, especially page 110, line 19 to page 111, line 10). Thus the art concludes that not all antibodies may have cell killing abilities via ADCC or CDC (Schlom, 'Monoclonal Antibodies: They're More and Less Than You Think', In: Molecular Foundations of Oncology, 1991, Samuel Broder, Ed, pages 95-134, especially page 106, first column, lines 17-19). Further, the specification teaches that the B305D antigen is present in patient sera, thus, bringing another variable into consideration, that of the presence of the target agent as a soluble protein in sera as opposed to the presence of the target antigen only on the cell surface.

The instant claims also encompass the induction of an anti-idiotypic immune response after administration of antibodies. The art teaches that the induction of the anti-idiotypic antibodies in animal models is effective against transplanted tumors, but that the induction of the idiotypic network in patients with solid tumors fails to produce substantial clinical results (abstract of Euhus et al, Surgery, Gynecology and Obstetrics, 1992, Vol. 175, pp. 89-96). It is reasonable to conclude that without auxiliary teachings or objective evidence in the specification, the induction of an anti-idiotypic immune response against the instant recognition molecules would exhibit the same lack or clinical response as previous attempts in the art.

There is no evidence of an induction of activation induced cell death by the binding of the recognition molecules of the invention to an antigen. Activation-Induced Cell Death (AICD) is a phenomenon which is active in hematopoietic cells and not normally associated with non-hematopoietic cells (Green et al, Immunological Reviews, 2003, Vol. 193, pp. 70-81). There are no teachings in the specification nor any art of record to indicate that the cognate antigen has structural or functional correlation with antigens which induce activation-induced cell death, such as CD40. The specification does not provide any teachings or guidance for how to make an antibody which would be directly toxic to breast tumor cells, and because it is unlikely that said recognition molecule would evoke a similar activation induced cell death as an anti-CD 40 antibody, one of skill in the art would be subject to undue experimentation in order to make such an antibody to use in the broadly drawn instant method of claim 13.

Given the unreliability of the art with respect to the induction of direct cellular toxicity akin to AICD, an anti-idiotypic immune response, ADCC, CDC or cytotoxicity as a result of delivery of a cytotoxic moiety, one of skill in the art would be forced into undue experimentation

in order to carry out the broadly claimed methods or to use the composition comprising an immunostimulant.

Claims 74, 75, 77, 78, 79 are rejection under 102(b) as being anticipated by the abstract of Karten (Hybridoma, 1995, Vol. 14, pp. 37-44).

Claim 74 is drawn to a molecule comprising an amino acid sequence which contains SEQ ID NO:1 and SEQ ID NO:2 or 3 and SEQ ID NO:4, 5 or 6. Claim 75 embodies the molecule of claim 74 further comprising SEQ ID NO:7, 8 or 9; and 10, 11 and :SEQ ID NO:12 or 13. Claim 77 embodies the recognition molecule of claim 74 wherein the molecule comprises a combination of molecules found listed in the claim. Claim 78 is drawn to the recognition molecule of claim 74 wherein said molecule is an immunoglobulin of the IgG, IgM, IgA, IgE, IgD and/or subclasses et al. Claim 79 is drawn in part to a construct comprising the recognition molecule of claim 74 and (i) immunoglobulin or (xii) immunoeffectors..

The abstract of Karsten discloses a monoclonal antibody which specifically binds both anomeric forms of the TF alpha and TF beta antigens, which is the same binding specificity as indicated in the instant specification on page 6, lines 16-18). The reference does not specifically teach that the antibody has the same hypervariable regions as the instant recognition molecules. However, the claimed molecules appear to be the same as the prior art antibody in terms of epitope binding absent a showing of unobvious differences. The Office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See *In re Best* 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray* 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

All claims are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10-6:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Karen A Canella/

Primary Examiner, Art Unit 1643